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NCI Launches New Initiative to Identify Genetic Risk Factors for Breast and Prostate Cancer

The National Cancer Institute (NCI), part of the National Institutes of Health, today launched an initiative to identify genetic alterations that make people susceptible to prostate and breast cancer, two of the most commonly diagnosed cancers in the United States. Cancer Genetic Markers of Susceptibility (CGEMS) is a three-year initiative, funded for $14 million, that will conduct scans of the entire human genome (genotyping) to identify common, inherited gene mutations that increase the risks for breast and prostate cancer.

The initiative will begin with the scanning of a total of 2,500 samples from men who have been diagnosed with prostate cancer, and men who have not. San Diego-based Illumina Inc. will conduct the rapid genotyping for the project. The most common human genetic variations that occur in humans are called single nucleotide polymorphisms or SNPs.

Previous studies have successfully identified single gene mutations that cause cancer or are linked to other inherited diseases. These studies have provided early insights into potential mechanisms of inherited cancer susceptibility, but these mutations are rare in the general population and directly related to only a small proportion of human cancer. In fact, most human cancer risk appears to be due, at least in part, to mutations that have low penetrance, meaning that they convey a low risk for cancer, but combinations of these mutations increase risk. One of the main goals of CGEMS is to identify genetic alterations that contribute to cancer risk, particularly the common low-penetrance, low-risk mutations. These alterations are also often referred to as susceptibility or modifier genes, since it is thought that they affect risk by increasing or decreasing a person's susceptibility to the cancer-causing effects of environmental and lifestyle exposures.

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Recent advances, such as the sequencing of the human genome and the development of technologies for very large-scale SNP genotyping, now make it possible to use common variants across the entire genome to map the low-penetrance gene mutations most often involved in an individual's risk of cancer. What makes CGEMS and other association studies different from candidate gene studies is that these association studies investigate the entire genome, with no assumptions about which alterations cause prostate or breast cancer. In addition, CGEMS has incorporated important follow-up studies in its design. The promising SNPs will then be analyzed and validated in a series of large, population-based studies. The validated SNPs will be further investigated to develop new strategies for prevention, earlier detection, and treatment of these cancers.

"The mapping of the human genome opened new frontiers of science. Projects like The National Cancer Institute's CGEMS, and the collaboration between NCI and the National Human Genome Research Institute on The Cancer Genome Atlas, will expand our knowledge and understanding of the genetics of disease, said NIH Director Elias A. Zerhouni, M.D.

"The CGEMS initiative represents the largest, comprehensive undertaking to identify the genetic risk factors for two cancers that take the lives of a combined total of more than 70,000 men and women every year," said NCI Deputy Director Anna D. Barker, Ph.D. "This project promises to provide a needed database to support the development of novel strategies for the early detection and prevention of these diseases."

Coordinated through NCI's Division of Cancer Epidemiology and Genetics, its Core Genotyping Facility, and its Office of Cancer Genomics, CGEMS will draw upon the expertise of scientists both within and outside NCI. The initiative will use the latest genetic technologies and scan the human genome by analyzing as many as 500,000 or more SNPs in each cancer case or control individual.

"CGEMS is among the first large whole genome scanning projects in cancer, and we are hopeful that its results will provide promising new insights into understanding genetic risk and common cancers, like breast and prostate cancer," stated Stephen J. Chanock, M.D., director of NCI's Advanced Technology Center Core Genotyping Facility.

"For many years, we've known that genetics contribute to an individual's risk of cancer. Capitalizing on the extraordinary momentum generated by advances in human genomic research, CGEMS is truly a different approach," explained David Hunter, M.D. an NCI Eminent Scholar and professor of cancer prevention at the Harvard School of Public Health.

To facilitate and encourage the development of this new research, CGEMS will make the data available to the entire cancer research community via NCI's caBIG™ (the cancer Biomedical Informatics Grid), available at http://cabig.nci.nih.gov/.

There were an estimated 232,090 new prostate cancer cases and 211,240 new breast cancer cases in the United States in 2005. Prostate cancer is the second leading cause of cancer-related death in men, and breast cancer is the second leading cause of cancer-related death in women. In the United States alone, in 2005, prostate cancer took the lives of an estimated 30,350 men, and breast cancer claimed the lives of approximately 40,410 women.

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For more information about cancer, please visit the NCI Web site at http://www.cancer.gov, or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).

For more information about the Cancer Genetic Markers of Susceptibility initiative, please visit http://cgems.cancer.gov.